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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,397	02/16/2001	Altaf A. Lal	6395-57049	4907

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	26

DATE MAILED: 10/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application N .	Applicant(s)	
	09/763,397	LAL ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears n the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,10 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,10 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 February 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. This Office Action is responsive to Applicant's amendment and response filed June 23, 2003 and August 4, 2003. Claims 1, 3, 5 and 10 have been amended. Claim 13 has been added.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Rejections Maintained

3. The rejection of claims 1, 3, 5-6 and newly submitted claim 13 under 35 U.S.C. 102(b) is maintained for the reasons set forth on page 3-4, paragraph 6 of the previous Office Action.

The rejection was on the grounds that Tine et al teach the highly attenuated NYVAC vaccinia strain has been utilized to develop a multiantigen, multistage vaccine candidate for malaria. Tine et al teach gene encoding seven *Plasmodium falciparum* antigen derived from the sporozoite, liver, blood and sexual stages of parasite lifecycle were inserted into a single NYVAC genome to generate NYVAC-Pf7. Tine et al teach that the genes that encode seven *Plasmodium falciparum* antigens derived from circumsporozoite protein, sporozoite surface protein, liver stage antigen 1, merozoite surface antigen, serine repeat antigen, apical membrane antigen 1 (i.e. T cell epitope) and 25kDa sexual-stage antigen. Tine et al teach that each of the seven antigens were expressed in HYVAC-Pf7-infected culture cells and the genotypic and phenotypic stability of the recombinant virus was demonstrated (see the Abstract). Tine et al teach that five of the seven *P. falciparum* antigens expressed by NYVAC-Pf7 are localized on the surface of infected culture cells (page 3839, 2nd column). Tine et al suggest that a NYVAAC recombinant expressing a constellation of seven *P. falciparum* antigens could provide a vaccine candidate with the potential to elicit immunity directed against multiple stages in the malarial life cycle (page 3836, 2nd column). The sequences of the epitopes from each of the life cycles would be inherent in the teachings of the prior art.

Applicant urges that Tine et al teach the insertion of genomic or cDNA copies of the genes encoding CSP, PfSSP2, a repeatless ~~from~~ form of LSA1, MSP1, SERA, AMAI and Pfs25 at four defined sites in the NYVAC genome. Applicant urges that the proteins were under the control of separate promoters and were separately transcribed. Applicant urges that amended claim 1 (and dependent claims 5, 6 and 10) recites a single recombinant protein comprising peptides from two or more stages in a life cycle of *P. falciparum*. Applicant urges that Tine et al teach the expression of multiple proteins each of which is from a particular life stage of *P. falciparum*. Applicant further urges that Tine et al do not teach SEQ ID NO: 2.

Applicant's arguments filed June 23, 2003 have been fully considered but they are not persuasive. It is the Examiner's position that Applicant is arguing process limitations and the claimed invention is drawn to a recombinant protein (a product). Tine et al teach a highly attenuated NYVAC vaccinia virus strain that has been utilized to develop a multiantigen, multistage vaccine candidate for malaria. Tine et al teach that the antigens derived from different lifecycles of *Plasmodium falciparum* were inserted into a single NYVAC genome to generate NYVAC-Pf7. The sequences of the epitopes from each of the life cycles would be inherent in the teachings of the prior art. The product of the prior art reference appears to be the same product claimed by the applicant because they appear to possess the same functional characteristics, (i.e. a recombinant protein). The production of a product by a particular process does not impart novelty or unobviousness to a

product when the same product is taught by the prior art. This is particularly true when properties of the product are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPO 964 (CAFC 1985); In re Marosi, 218 USPO 289, 29222-293 (CAFC 1983); In re Brown, 173 USPO 685 (CCPA 1972). The claimed recombinant protein is the same as the recombinant protein of the prior art since Applicant has provided no side-by-side comparison to show that the claimed recombinant protein differs from that of the prior art.

4. The rejection of claims 1, 3-6 and newly submitted claim 13 under 35 U.S.C. 103(a) is maintained for the reasons set forth on page 3-6, paragraph 6 of the previous Office Action.

The rejection was on the grounds that that Tine et al teach the highly attenuated NYVAC vaccinia strain has been utilized to develop a multiantigen, multistage vaccine candidate for malaria. Tine et al teach gene encoding seven *Plasmodium falciparum* antigen derived from the sporozoite, liver, blood and sexual stages of parasite lifecycle were inserted into a single NYVAC genome to generate NYVAC-Pf7. Tine et al teach that the genes that encode seven *Plasmodium falciparum* antigens derived from circumsporozoite protein, sporozoite surface protein, liver stage antigen 1, merozoite surface antigen, serine repeat antigen, apical membrane antigen 1 (i.e. T cell epitope) and 25kDa sexual-stage antigen. Tine et al teach that each of the seven antigens were expressed in HYVAC-Pf7-infected culture cells and the genotypic and phenotypic stability of the recombinant virus was demonstrated (see the Abstract). Tine et al teach that five of the seven *P. falciparum* antigens expressed by NYVAC-Pf7 are localized on the surface of infected culture cells (page 3839, 2nd column). Tine et al suggest that a NYVAAC recombinant expressing a constellation of seven *P. falciparum* antigens could provide a vaccine candidate with the potential to elicit immunity directed against multiple stages in the malarial life cycle (page 3836, 2nd column).

Tine et al do not teach the use of a polyhistidine.

Schmitt et al teach affinity purification of histidine-tagged proteins (see the Title). Schmitt et al teach that the expression of recombinant proteins is a standard technique in molecular biology and a wide variety of prokaryotic as well as eukaryotic expression systems are currently in use. Schmitt et al teach that a

limiting step is often that the purification of the expressed recombinant protein that yield low expression levels are employed (see the Abstract). Schmitt et al teach that short amino acid sequences can be fused to the recombinant protein as a tag (page 223). Schmitt et al teach that a stretch of 6 histidine residues (His-tag) linked to the N- or C-terminal part of a recombinant protein is sufficient to allow a high expression of purified protein
(page 229).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the histidine-tag as taught by Schmitt et al to the recombinant poxvirus vectored multiantigen of Tine et al because Tine et al suggest that a NYVAC recombinant expressing a constellation of seven *P. falciparum* antigens could provide a vaccine candidate with the potential to elicit immunity directed against multiple stages in the malarial life cycle (page 3836, 2nd column). It well known in the art to express, characterize and purify recombinant proteins. It is well known in the art to use signal proteins to express recombinant proteins and to use polyhistidine tags to purify recombinant proteins. Schmitt et al teach a stretch of 6 histidine residues (His-tag) linked to the N- or C-terminal part of a recombinant protein is sufficient to allow purification of the recombinant protein (page 229). It would have been expected barring evidence to the contrary, that the addition of a His-tag to recombinant proteins would allow for high expression of purified protein. The addition of the His-tag is well within the level of skill in the art.

Applicant urges that Tine et al do not teach or suggest all elements in claims 1 and 3-6. Applicant urges that Schmitt et al do not teach or suggest the claim elements lacking in Tine et al. Applicant urges that all of the claim limitations are not taught and therefore a *prime facie* case of obviousness has not been established. Applicant urges that new claim 13 depends from claim 1 and avoids Tine et al and Tine et al in view of Schmitt et al for the same reasons stated for claim 1.

Applicant's arguments filed June 23, 2003 have been fully considered but they are not persuasive. It is the Examiner's position that the combination of references teach the claimed invention. The claims are drawn to a recombinant protein. Tine et al teach a highly attenuated NYVAC vaccinia virus strain that

has been utilized to develop a multiantigen, multistage vaccine candidate for malaria. Tine et al teach that the antigens derived from different lifecycles of *Plasmodium falciparum* were inserted into a single NYVAC genome to generate NYVAC-Pf7. Tine et al do not teach polyhistidine tags. However, Schmitt et al teach that polyhistidine tags are attached to recombinant proteins to express and characterize the recombinant proteins. Therefore, it would have been obvious to add the polyhistidine tags of Schmitt et al to the recombinant protein of Tine et al to better express and characterize the recombinant protein.

In response to applicant's argument that no *prima facie* case has been established, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). There is nothing on the record to show that the combination of teachings would not suggest the claimed invention. Therefore, the teachings of Tine et al combined with the teachings of Schmitt et al suggest the claimed invention.

5. The rejection of claim 10 under 35 U.S.C. 102(b) is maintained for the reasons set forth on pages 7-8, paragraph 8 of the previous Office Action.

The rejection was on the grounds that Tine et al teach the highly attenuated NYVAC vaccinia strain has been utilized to develop a multiantigen,

multistage vaccine candidate for malaria. Tine et al teach gene encoding seven *Plasmodium falciparum* antigen derived from the sporozoite, liver, blood and sexual stages of parasite lifecycle were inserted into a single NYVAC genome to generate NYVAC-Pf7. Tine et al teach that the genes that encode seven *Plasmodium falciparum* antigens derived from circumsporozoite protein, sporozoite surface protein, liver stage antigen 1, merozoite surface antigen, serine repeat antigen, apical membrane antigen 1 (i.e. T cell epitope) and 25kDa sexual-stage antigen. Tine et al teach that each of the seven antigens were expressed in HYVAC-Pf7-infected culture cells and the genotypic and phenotypic stability of the recombinant virus was demonstrated (see the Abstract). Tine et al teach that five of the seven *P. falciparum* antigens expressed by NYVAC-Pf7 are localized on the surface of infected culture cells (page 3839, 2nd column). Tine et al suggest that a NYVAAC recombinant expressing a constellation of seven *P. falciparum* antigens could provide a vaccine candidate with the potential to elicit immunity directed against multiple stages in the malarial life cycle (page 3836, 2nd column). The sequences of the epitopes from each of the life cycles would be inherent in the teachings of the prior art. Tine et al teach the safety and the immunogenicity in nonhuman primates (page 3840, 2nd column). It would be inherent that the recombinant NYVAC-Pf7 vaccine formulations given to nonhuman primates would contain a pharmaceutically acceptable carrier.

Since the Office does not have the facilities for examining and comparing applicant's protein composition with the protein composition of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein composition of the prior art does not possess the same material structural and functional characteristics of the claimed protein composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that Tine et al teach the insertion of genomic or cDNA copies of the genes encoding CSP; PfSSP2, a repeatless form of LSA1, MSP1, SERA, AMAI and Pfs25 at four defined sites in the NYVAC genome. Applicant urges that the proteins were under the control of separate promoters and were separately transcribed. Applicant urges that amended claim 1 (and dependent claims 5, 6 and 10) recite a single recombinant protein comprising peptides from two or more stages in a life cycle of *P. falciparum.* Applicant urges that Tine et al teach the expression of multiple proteins each of which is from a particular life

stage of *P. falciparum*. Applicant further urges that Tine et al do not teach SEQ ID NO: 2.

Applicant's arguments filed June 23, 2003 have been fully considered but they are not persuasive. It is the Examiner's position that Applicant is arguing process limitations and the claimed invention is drawn to a composition comprising a recombinant protein (a product). Tine et al teach a highly attenuated NYVAC vaccinia virus strain that has been utilized to develop a multiantigen, multistage vaccine candidate for malaria. Tine et al teach that the antigens derived from different lifecycles of *Plasmodium falciparum* were inserted into a single NYVAC genome to generate NYVAC-Pf7. Tine et al suggest that a NYVAAC recombinant expressing a constellation of seven *P. falciparum* antigens could provide a vaccine candidate with the potential to elicit immunity directed against multiple stages in the malarial life cycle (page 3836, 2nd column). Tine et al demonstrated the safety and the immunogenicity of NYVAC-Pf7 in nonhuman primates (page 3840, 2nd column). The sequences of the epitopes from each of the life cycles would be inherent in the teachings of the prior art. The recombinant NYVAC-Pf7 vaccine formulations given to nonhuman primates would inherently contain a pharmaceutically acceptable carrier. The product of the prior art reference appear to be the same of the product claimed by the applicant because they appear to possess the same functional characteristics, (i.e. a composition comprising the recombinant protein). The production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is

taught by the prior art. This is particularly true when properties of the product are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPO 964 (CAFC 1985); In re Marosi, 218 USPO 289, 29222-293 (CAFC 1983); In re Brown, 173 USPO 685 (CCPA 1972). The claimed composition comprising the recombinant protein is the same as the composition comprising the recombinant protein of the prior art since Applicant has provided no side-by-side comparison to show that the claimed composition differs from that of the prior art.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
October 8, 2003

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
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